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(72) Inventor: **Siddiqi, Salman H.**
Sparks, Maryland 21152 (US)

(74) Representative: **Weber, Thomas, Dr. et al**
Patentanwälte von Kreisler-Selting-Werner,
Deichmannhaus am Dom,
Bahnhofsvorplatz 1
50667 Köln (DE)

(30) Priority: **10.01.2002 US 41667**

(71) Applicant: **Becton, Dickinson and Company**
Franklin Lakes, New Jersey 07417-1880 (US)

(54) **Methods and devices for collecting and preparing specimens for detection of mycobacteria and their antigens**

(57) Methods and articles of manufacture are disclosed for detecting a secreted mycobacterial antigen directly in a biological sample obtained from a mammalian subject without substantial replication of mycobacterial cells in the sample. This method comprises contacting an antibody that specifically binds to the secreted mycobacterial antigen with the sample, or a fraction thereof, under conditions such that the antibody specifically binds to secreted mycobacterial antigen in the sample, thereby forming a specific complex of the antibody with the secreted mycobacterial antigen. This method further comprises detecting the presence, absence or amount of specific complex of the antibody with the secreted mycobacterial antigen in the sample. In this method the presence of this specific complex indicates the presence of the secreted mycobacterial antigen in

the sample. The invention method is particularly useful for detecting MPB64 antigen of *M. bovis* or MPT64 antigen of *M. tuberculosis* in biological samples from a human subject suspected of having tuberculosis, particularly for sputum samples from such subjects. Prior to contacting the sample with an antibody that specifically binds to MPB64 antigen or MPT64 antigen, a mucolytic or liquifying agent, preferably containing a disulfide bond reducing agent, and optionally a decontaminating agent, is added to the sample. One preferred disulfide bond reducing agent is N-acetyl-L-cysteine (NALC) and advantageously this agent is added to the sample to achieve a concentration in the sample that is substantially greater than 0.25% (w/v), for instance, about 2.5% (w/v).

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EUROPEAN SEARCH REPORT

Application Number
EP 03 00 0366

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
D,X	US 6 245 331 B1 (BELISLE JOHN T ET AL) 12 June 2001 (2001-06-12)	1,3,4	G01N33/569
Y	* column 21, lines 38-67 * * column 9, lines 15-30 *	2,5	
X	EP 0 273 333 A (BIOTEST AG) 6 July 1988 (1988-07-06)	1,3,4,8	
Y	* the whole document *	6,7	
X	WO 97/34149 A (SVENSON STEFAN) 18 September 1997 (1997-09-18)	1,4	
X	WO 00/73345 A (PROMEGA CORP) 7 December 2000 (2000-12-07) * page 6, line 4 - page 7, line 6 * * page 23, line 30 - page 25, line 6; claims 36-48; example 2 *	1,3,4	TECHNICAL FIELDS SEARCHED (Int.Cl.7) G01N
D,X	ABE CHIYOJI ET AL: "Simple and rapid identification of the Mycobacterium tuberculosis complex by immunochromatographic assay using anti-MPB64 monoclonal antibodies." JOURNAL OF CLINICAL MICROBIOLOGY, vol. 37, no. 11, November 1999 (1999-11), pages 3693-3697, XP002241048 ISSN: 0095-1137	8	
Y	* page 3693, column 2, paragraph 2 - page 3694, column 2, paragraph 3 *	2,5-7	
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The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 1 March 2004	Examiner Vanmontfort, D
CATEGORY OF CITED DOCUMENTS T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			

EPO FORM 1503 03/82 (P04C01)



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EUROPEAN SEARCH REPORT

Application Number
EP 03 00 0366

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
D,Y	<p>ROCHE P W ET AL: "Expression of Mycobacterium tuberculosis MPT64 in recombinant Myco. smegmatis: Purification, immunogenicity and application to skin tests for tuberculosis." CLINICAL AND EXPERIMENTAL IMMUNOLOGY, vol. 103, no. 2, 1996, pages 226-232, XP009010785 ISSN: 0009-9104 * abstract *</p>	2,5-7	
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A	<p>----- WO 92/14156 A (DYNAGEN INC) 20 August 1992 (1992-08-20) * example 1 *</p>	6,7	
P,X	<p>----- DATABASE WPI Section Ch, Week 200243 Derwent Publications Ltd., London, GB; Class B04, AN 2002-398911 XP002242833 & JP 2002 062299 A (KYOWA MEDEX KK) 28 February 2002 (2002-02-28) * abstract *</p> <p>-----</p>	1-5	
The present search report has been drawn up for all claims			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Place of search Munich		Date of completion of the search 1 March 2004	Examiner Vanmontfort, D
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			

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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- ☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):
- ☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- ☒ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
- ☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.
- ☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:
- ☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:



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LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 03 00 0366

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-5, 8-10

Method for detection of secreted mycobacterial antigen in a biological sample; Method for detection of an infection of a mammalian subject by a mycobacterial species that produces a secreted mycobacterial antigen by testing a biological sample; An article of manufacture for the detection of a mycobacterial antigen.

2. claims: 6, 7

A method of pretreatment of samples which will be subjected to a method of detection of secreted mycobacterial antigen.

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 03 00 0366

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
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01-03-2004

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82